Figure 2. Estimated Comparative Daily Dosages for Inhaled Corticosteroids (Updates EPR-2 Figure 3–5b)

Drug	Low Daily Dose		Medium Daily Dose		High Daily Dose	
	Adult	Child*	Adult	Child*	Adult	Child*
Beclomethasone CFC 42 or 84 mcg/puff	168–504 mcg	84–336 mcg	504–840 mcg	336–672 mcg	> 840 mcg	> 672 mcg
Beclomethasone HFA 40 or 80 mcg/puff	80–240 mcg	80–160 mcg	240–480 mcg	160–320 mcg	> 480 mcg	> 320 mcg
Budesonide DPI 200 mcg/inhalation	200–600 mcg	200–400 mcg	600–1,200 mcg	400–800 mcg	> 1,200 mcg	> 800 mcg
Inhalation suspension for nebulization (child dose)		0.5 mg		1.0 mg		2.0 mg
Flunisolide 250 mcg/puff	500–1,000 mcg	500–750 mcg	1,000–2,000 mcg	1,000–1,250 mcg	> 2,000 mcg	> 1,250 mcg
Fluticasone MDI: 44, 110, or 220 mcg/puff	88–264 mcg	88–176 mcg	264–660 mcg	176–440 mcg	> 660 mcg	> 440 mcg
DPI: 50, 100, or 250 mcg/inhalation	100–300 mcg	100–200 mcg	300–600 mcg	200–400 mcg	> 600 mcg	> 400 mcg
Triamcinolone acetonide 100 mcg/puff	400–1,000 mcg	400–800 mcg	1,000–2,000 mcg	800–1,200 mcg	> 2,000 mcg	> 1,200 mcg

* Children ≤12 years of age

Note

- The most important determinant of appropriate dosing is the clinician's judgment of the patient's response to therapy. The clinician must monitor the patient's response on several clinical parameters and adjust the dose accordingly. The stepwise approach to therapy emphasizes that once control of asthma is achieved, the dose of medication should be carefully titrated to the minimum dose required to maintain control, thus reducing the potential for adverse effect.
- Comparative dosages in the EPR-2 were based on a limited number of published comparative clinical trials and extrapolation of differences in topical potency and lung delivery. This updated comparative dosage chart is based on review of recently published clinical trials involving more than 5,000 patients and published reviews (Barnes PJ et al. 1998; Kelly 1998; Pedersen 1997). The key differences from the EPR-2 include a higher dosage of budesonide and recommendations for two newly available medications: beclomethasone HFA and budesonide suspension for nebulization. The rationale for these changes is summarized as follows:
  - The high dose is the dose that appears likely to be the threshold beyond which significant hypothalamic-pituitary-adrenal (HPA) axis suppression is produced, and, by extrapolation, the risk is increased for other clinically significant systemic effects if used for prolonged periods of time (Martin et al. 2002; Szefler et al. 2002).
  - The low and medium dose reflects findings from dose-ranging studies in which incremental efficacy within the low-to-medium dose ranges was established without increased systemic effect as measured by overnight cortisol excretion. The studies demonstrated a relatively flat dose-response curve for efficacy at the medium-dose range; that is, increasing the dose to high-dose range did not significantly increase efficacy but did increase systemic effect (Martin et al. 2002; Szefler et al. 2002).
  - The dose for budesonide dry powder inhaler (DPI) is based on recently available comparative data with other medications, rather than the comparison to budesonide metered-dose inhaler (MDI) that was used in the EPR-2. These new data, including a meta-analysis of seven studies, show that budesonide DPI is comparable to approximately one-half the microgram dose of fluticasone (Barnes NC et al. 1998; Nielsen and Dahl 2000).
  - The dose for beclomethasone HFA is one-half the dose for beclomethasone CFC, based on studies demonstrating that the different pharmaceutical properties of the medications result in enhanced lung delivery for the HFA (a less forceful spray from the HFA propellant and a reengineered nozzle that allows a smaller particle size) (Leach et al. 1998; Busse et al. 1999; Gross et al. 1999; Thompson et al. 1998).
  - The dose for budesonide nebulizer suspension is based on efficacy and safety studies (Baker et al. 1999; Kemp et al. 1999; Shapiro et al. 1998), but no comparative studies with other inhaled corticosteroids are available. It is noted that the efficacy studies did not demonstrate a clear or consistent dose-response, although the high dose of 2.0 mg was effective in a placebo-controlled study in 40 infants with severe asthma (de Blic et al. 1996). In a small open-label long-term safety study, the ACTH stimulated cortisols appeared lower in the 13 infants receiving the high dose of 2.0 mg budesonide compared to infants receiving lower doses, but this was not statistically significant due, perhaps, to the small study size (Scott and Skoner 1999).
- Some doses may be outside package labeling, especially in the high-dose range.
- MDI dosages are expressed as the actuater dose (the amount of the drug leaving the actuater and delivered to the patient), which is the labeling required in the United States. This is different from the dosage expressed as the valve dose (the amount of drug leaving the valve, not all of which is available to the patient), which is used in many European countries and in some scientific literature. DPI doses are expressed as the amount of drug in the inhaler following activation.